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(57) Abstract

A composition for use as an adhesive for dental prostheses, with an antiphlogistically active content of camomile extract, the use thereof and the preparation of a medicament on the basis thereof.

Adhesive for Dental Prostheses

The Invention relates to a novel composition for use as an adhesive for dental prosthesis, the use thereof and a process for the preparation of a medicament for preventing or alleviating inflammation in the oral mucosa region.

Although it is known that adhesives per se fulfil a preventive function, because they form a film on the prosthesis and in this way protect the sensitive mucosa against pressure points and inflammation, in the case of dental prosthesis wearers there are still pressure points and inflammation in the oral mucosa region. Thus, for reinforcing the preventative action there are prosthesis adhesives on the market, which contain as the anti-inflammatory active substance α-bisabolol which may be derived from camomile.

Throughout this specification, unless the context requires otherwise, the word "comprise", or variations such as "comprises" or "comprising", will be understood to imply the inclusion of a stated element, integer or step, or group of elements, integers or steps, but not the exclusion of any other element, integer or step, or group of elements, integers or steps.

Disclosure of The Invention

According to the invention there is provided a dental prosthesis adhesive composition characterized by comprising as the sole antiphlogistic material, 1-10 wt.% of an antiphlogistically active camomile extract content, and at least one active adhesive substance.

In one alternative, the composition can be in the form of a cream, ointment or gel and in this case the camomile extract is preferably in an oil-compatible preparation.

Preferably, the composition according to the invention contains 1 to 10, preferably 1 to 5, more preferably 1.5 to 3.5 and in particular approximately 2 wt. % camomile extract. The percentages are related to camomile constituents. When using camomile extracts with other active contents it would be necessary to adapt the camomile extract percentage in the adhesive.

Further according to the invention, there is provided a dental prosthesis adhesive composition comprising

i) 1 to 10 wt. % camomile extract,

ii) 30 to 60 wt. % of at least one active adhesive substance,

iii) 30 to 69 wt. % of a base for the cream, ointment or gel and

iv) optionally up to 2 wt. % of further additives such as flavouring agents, dyes and stabilizers.

Preferably the base for the cream, ointment or gel in the composition comprises a substance chosen from the group constituted by paraffin oil, sunflower oil, soy oil (that is to say soya bean oil), Vaseline and hydrophobic oleogels.

In another alternative, the composition according to the invention can be in the form of a powder. The camomile extract is then preferably in a pulverulent preparation and in particularly preferred manner in a spray-dried preparation.

Further according to the invention, there is provided a composition comprising 0.1 to 3.0, preferably 0.2 to 1.0 and in particular approximately 0.5 wt.% camomile extract, where the camomile extract is a preparation with approximately 50% camomile constituents.

Preferably such a composition comprises

a) 0.1 to 3.0 wt.% camomile extract,

b) 30 to 99.9 wt.% of at least one active adhesive substance and

c) optionally further additives such as flavouring agents (up to 2 wt.%), dyes (up to 0.1 wt.%), stabilizers (up to 1 wt.%) and/or free-flow aids/diluents (up to 40 wt.%).

It is preferable for the active adhesive substance in a composition according to the invention to be selected from the group comprising sodium carboxymethyl cellulose, sodium alginate, copolymer salts of methyl vinyl ether/maleic anhydride, polyvinyl acetate, polyvinyl pyrrolidone, hydroxyethyl cellulose, polyoxymethylene, polyacrylamides and mixtures thereof.

A composition according to the invention may in addition have added to the adhesive at least one further addition of an antiphlogistically active substance being a camomile extract constituent, such as α-bisabolol.

Further according to the invention, there is provided the use of camomile extract in an adhesive for dental prostheses for preventing or alleviating inflammation in the oral mucosa region.

Still further according to the invention there is provided a process for the preparation of a medicament for preventing or alleviating inflammation in the oral mucosa region, in which an antiphlogistically active quantity of camomile extract is mixed with at least one active adhesive substance.

It has surprisingly been found that the dental prosthesis adhesive compositions according to the invention have a better antiphlogistic action than the known adhesives which include only one constituent of camomile, α-bisabolol. Although the applicant does not wish to be bound by it, the hypothesis can be made that there is a synergistic action of the main constituents in the camomile extract, which surprisingly leads to said extract being antiphlogistically more active than α-bisabolol alone. The main camomile constituents, in addition to the α-bisabolol, which could play a further part here are azulenes (chamazulene, guajazulene), further sesquiterpene derivatives (bisabolol oxides A, B and C, bisabolone oxide A), and flavone glycosides (hyperoxide, rutin, luteolin-7-glucoside, apigenin-7-glucoside), cumarin and farnesene.

In addition, in a confidential consumer test it was found that unexpectedly the adhesive composition according to the invention with camomile extract was also better evaluated with respect to adhesion than other products. Finally, the superior drawability of the product according to the invention was established, which also indicates improved adhesion.

The invention is described in greater detail hereinafter by the following examples, which are in the form of preparation examples and test results concerning the anti-inflammatory/inflammation-preventing activity, as well as the improved adhesion of the adhesive composition according to the invention. In the drawings the figures are as follows:

Fig. 1 A graph representing the capillary cutaneous circulation in the case of three adhesive creams according to the invention and untreated skin surface (control), plotted against time.

Fig. 2 A graph showing the capillary cutaneous circulation in the preferred adhesive cream according to the invention (HM 239), two different comparison substances (HP1 and HP2) and the untreated skin surface (control), plotted against time.

Fig. 3 A diagram showing the confidential consumer test results with respect to the purchasing readiness of a product according to the invention and two comparison products.

Fig. 4 A diagram showing the confidential consumer test results with regards to the product performance overall for a product according to the invention and two comparison products.

Fig. 5 A diagram showing the confidential consumer test results relative to the general evaluation of a product according to the invention and two comparison products.

Fig. 6 A diagram showing the confidential consumer test results with respect to the adhesive action of a product according to the invention and two comparison products.

Fig. 7 A diagram comparing the drawability (in Newtons) for a product according to the invention and two comparison products.

Before going into detail on the different exemplified formulations, we wish to point out that in general any camomile extract is suitable within the scope of the present invention which has an antiphlogistic action, independently of the extracting agent and the camomile species (growing, part of the plant, cultivation area, etc.).

The prerequisite for use in the adhesive composition according to the invention is that the camomile extract is brought in a form that is compatible with an end product application form.

This for example means that when used in the form of a cream, gel or ointment, the hydrophilic solvents (alcohols, glycols) are removed and that the preparation is carried out with more hydrophobic and therefore more oil-compatible solvents, such as e.g. soy oil (soya bean oil) or sunflower oil.

In the following examples, the camomile extract used in Example 1 is Phytoconcentrol Camomile Oil-Soluble 2/066310 and that used in Example 2 is Neo-Extrapon camomile 2/060350 (both from Dragoco). Other suitable extracts in oil-compatible preparation are e.g. camomile extracts LS 2416 G (soy oil, ie soya bean oil), LS 2904 G (sunflower oil) or LS 3066 G (diisobutyl adipate) from Grau Aromatics (or corresponding products from Gattefossé GmbH e.g. Vegetol 4140).

Example 1: Preparation of an adhesive cream according to the invention

The following tables 1 and 2 give exemplified formulations for an adhesive cream with camomile extract, the products with the designations VM 196, HM 239 and HM 347 are in the particularly preferred range for the camomile extract content. The given formulations were used for the subsequently described tests. The camomile extract used was present in a preparation with approximately 10% camomile constituents.

TABLE 1

Constituents	VM.196	HM 239
Paraffin oil	31.88	32.88
Vaseline	12.00	12.00
Peppermint oil	0.10	0.10
Menthol	0.02	0.02
Camomile extract (oil-soluble)	3.00	2.00
Sodium carboxymethyl cellulose (high viscosity)	15.00	15.00
Sodium carboxymethyl cellulose (medium viscosity)	8.00	8.00

Poly(maleic acid/methyl vinyl ether) calcium / sodium salt	30.00	30.00

TABLE 2

Constituents	HM 347	HM 349
Paraffin oil	30.375	32.075
Vaseline	14.50	13.80
Peppermint oil	0.10	0.10
Menthol	0.02	0.02
Dye E 127	0.005	0.005
Camomile extract (oil-soluble)	2.00	1.00
Sodium carboyxmethyl cellulose (high viscosity)	15.00	15.00
Sodium carboxymethyl cellulose (medium viscosity)	8.00	8.00
Poly(maleic acid/methyl vinyl ether) calcium sodium salt	30.00	30.00

The preparation of the corresponding adhesive creams in each case took place in the following way.

A Unimix mixer was pre-heated to 38°C. On reaching the temperature the weighed quantities of paraffin oil, melted Vaseline and optionally dye were fed in. This was followed by the addition of a mixture, prepared on the previous day, of peppermint oil and menthol, as well as the camomile extract. The mixture was then stirred for 3 minutes at 50 r.p.m.

This was followed by the addition of the pulverulent adhesive raw materials by filling connection and accompanied by stirring in the following order: poly(maleic acid/methyl vinyl ether) calcium sodium salt, sodium carboxymethyl cellulose (high viscosity) and sodium carboxymethyl cellulose (medium viscosity).

After adding all the powder components the mixture was stirred for a further 60 minutes at 50 r.p.m. until all the constituents were homogeneously distributed.

Example 2: Preparation of an adhesive powder according to the invention

A formulation for an adhesive powder with a dried, pulverized camomile extract (having an approximately 50% camomile constituent content) was made up as follows:

99.5%	sodium alginate DAB
0.5%	Neo-Extrapon camomile 2/060350 (Dragoco)
	or
50%	sodium carboxymethyl cellulose DAB
49.7%	sodium alginate DAB
0.3%	Neo-Extrapon camomile 2/060350 (Dragoco).

The pulverized active substances were weighed in and transferred into a suitable container (e.g. conical worm mixture or helical belt mixer). Mixing took place until all the active substances were completely homogeneously distributed.

Example 3: Testing the anti-inflammatory/inflammation-inhibiting activity of the adhesive to the invention

For the activity test described in greater detail hereinafter comparison took place between the adhesive creams prepared according to example 1, a standard commercial product (HP 1), a commercial product with α-bisabolol (HP 2) and the untreated skin surface (control).

Testing took place on volunteer test persons, under secrecy provisions, with a healthy skin. Using a solar simulator, irradiation took place until the erythema threshold was reached. Immediately following radiation the previously divided up test areas were treated with the formulations (control: untreated).

Application of the test preparations took place under occlusion, in order to come close to the conditions of the oral mucosa. A subsequent treatment took place after 3, 6, 9, 24 and 48 hours.

The antiphlogistic activity was tested by measurements of capillary cutaneous circulation using the laser-Doppler flow meter. The lower the cutaneous circulation values the lower the erythema/irritation effects and the higher the antiphlogistic activity of the test product.

This process has been established as an investigation model for determining the antiphlogistic activity. It is possible to transfer the results from the normal skin to the oral mucosa, because as a result of easier resorption conditions in the oral mucosa, a reinforcement of the antiphlogistic properties is to be expected. The test results are compared in figs. 1 and 2.

Fig. 1 shows that even a 1% camomile extract content reveals a superior action compared with the control, but that an even more pronounced improvement results from increasing the content to 2%.

A further increase in the camomile extract content to 3% leads to no further improvement of the antiphlogistic activity and in fact causes a slight deterioration compared with the product having a 2% camomile extract content.

Fig. 2 compares the untreated skin surface (control), products HP 1 and HP 2 and the product according to the invention with the optimum camomile extract content. The superior action of the adhesive according to the invention is very apparent.

Example 4: Testing the adhesion of the adhesive cream according to the invention

In the following tests comparisons took place between the standard adhesive cream product (HP 1) known from example 3, the commercial product with α-bisabolol (HP 2) known from example 3 and the product according to the invention (VP) (corresponding to product Hm 239 of example 3) in a confidential consumer test and in a drawability test.

The confidential consumer test was carried out in such a way that the test products were concealed and in monadic manner by the consumer at home. The consumer was given brief instructions for use. Each group consisted of 60 persons, all of whom were adhesive cream or adhesive gel users.

The evaluation scale extended from 1 to 5 and 5 represented the maximum number of points attainable. The results are shown in figs. 3 to 6 in the categories readiness to purchase, product performance overall, general evaluation and adhesive action.

The product according to the invention with camomile extract revealed superior values in all categories. Of greatest interest are the adhesive action results of fig. 6.

Fig. 7 compares the results of drawability test for the three aforementioned products. The test was performed in such a way that the test substance was placed on a plate, comprising a commercial prosthesis plastic material, weighed in and mixed with a clearly defined quantity of water. This plate was screwed into the tensile and compressive force measuring instrument (Erichsen 391). At the top was also screwed in a plate made from a commercial prosthesis plastic material, but which was additionally provided with an underlining material support which remained soft. The two plates were then compressed under clearly defined conditions. After a clearly defined time the force (in N) was measured, which was necessary for pulling apart the two plates. The read off value represents the drawability in N.

THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:-

1. A dental prosthesis adhesive composition characterized by comprising as the sole antiphlogistic material, 1-10 wt.% of an antiphlogistically active camomile extract content, and at least one active adhesive substance.

2. A composition according to claim 1, in which the composition is in the form of a cream, ointment or gel.

3. A composition according to claim 1 or claim 2, in which the camomile extract is present in an oil-compatible preparation.

4. A composition according to any one of the preceding claims, in which the content of camomile extract is 1 to 5 wt.%.

5. A composition according to any one of the preceding claims, in which the content of camomile extract is 1.5 to 3.5 wt.%.

6. A composition according to any one of the preceding claims, in which the content of camomile extract is approximately 2 wt.%.

7. A composition according to any one of the preceding claims, in which the content of camomile extract is based on a camomile extract in a preparation with approximately 10% camomile constituents.

8. A denture fixing composition in the form of a cream, ointment or gel, comprising

i) 1 to 15% of an antiphlogistically active camomile extract,

ii) 30 to 60 wt.% of at least one active adhesive substance,

iii) 30 to 69 wt.% of a base for the cream, ointment or gel and

(iv) optionally up to 2 wt.% of further additives comprising flavouring agents, dyes and stabilizers.

9. A composition according to any one of the claims 2 to 8, characterized in that the base for the cream, ointment or gel is chosen from the group comprising paraffin oil, sunflower oil, soy oil (soya bean oil), Vaseline and hydrophobic oleogels.

10. A composition according to claim 1, in which the composition is present as a powder.

11. A composition according to claim 10, in which the camomile extract is present in a pulverulent preparation.

12. A composition according to claim 11, characterized in that the camomile extract is present in a spray-dried preparation.

13. A composition according to any one of claims 10 to 12, in which the content of camomile extract is based on a camomile extract in a preparation with approximately 50% camomile constituents.

14. A powdered denture fixing composition, comprising

a) 0.1 to 3.0 wt.% of an antiphlogistically active camomile extract,

b) 30 to 99.9 wt.% of at least one active adhesive substance and

c) optionally further additives comprising flavouring agents (up to 2 wt.%), dyes (up to 0.1 wt.%), stabilizers (up to 1 wt.% and/or free-flow aids/diluents (up to 40 wt.%).

15. A composition according to claim 14, in which the content of camomile extract is 0.2 to 1.0 wt.%.

16. A composition according to either one of claims 14 and 15 in which the content of camomile extract is approximately 0.5 wt.%.

17. A composition according to any one of claims 1 to 16, in which the active adhesive substance is selected from the group comprising sodium carboxymethyl cellulose, sodium alginate, copolymer salts methyl vinyl ether/maleic anhydride, polyvinyl acetate, polyvinyl pyrrolidone,

hydroxyethyl cellulose, polyoxymethylene, polyacrylamides and mixtures thereof.

18. A composition according to any one of the preceding claims, in which the composition further contains at least one further antiphlogistically active substance being a camomile extract constituent.

19. A composition according to claim 18, wherein the camomile extract constituent is α-bisabolol.

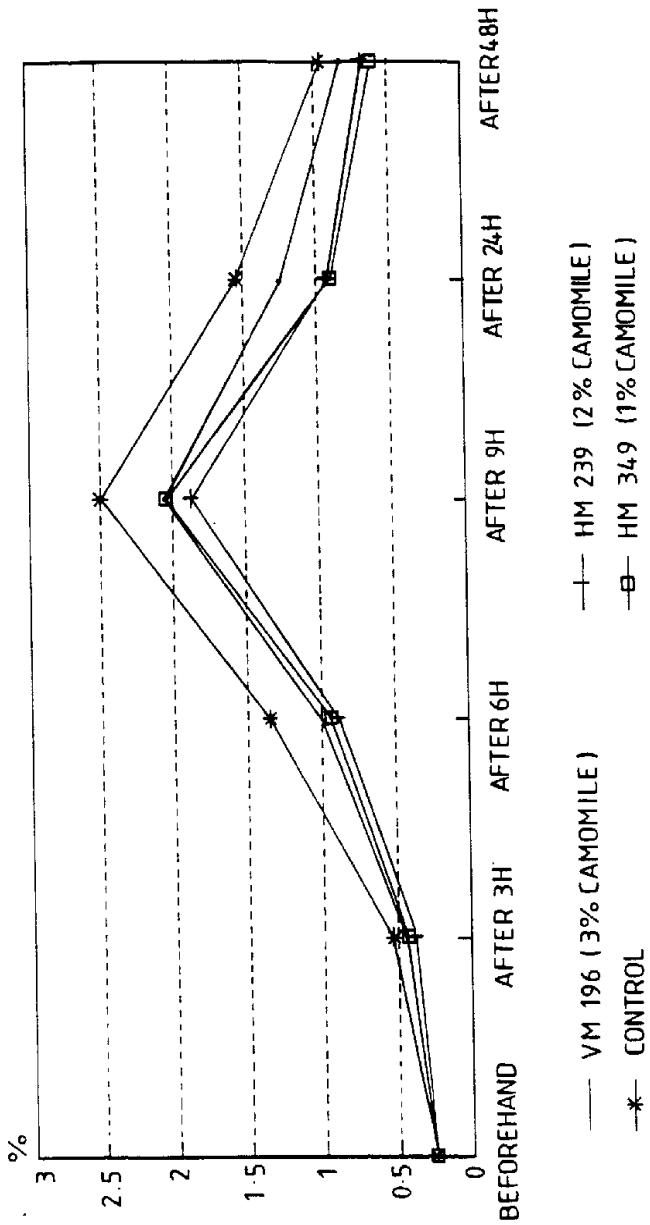
20. Use of camomile extract in an adhesive for dental prostheses for preventing or alleviating inflammation in the oral mucosa region wherein 1 to 10 wt.% of camomile extract is included in the adhesive.

21. A process for the preparation of a medicament for preventing or alleviating inflammation in the oral mucosa region, characterized by mixing 1 to 10 wt.% of an antiphlogistically active quantity of camomile extract with at least one active adhesive substance.

DATED this 9th day of August 1999

KUKIDENT GMBH
Patent Attorneys for the
Applicant:

F.B. RICE & CO.


%
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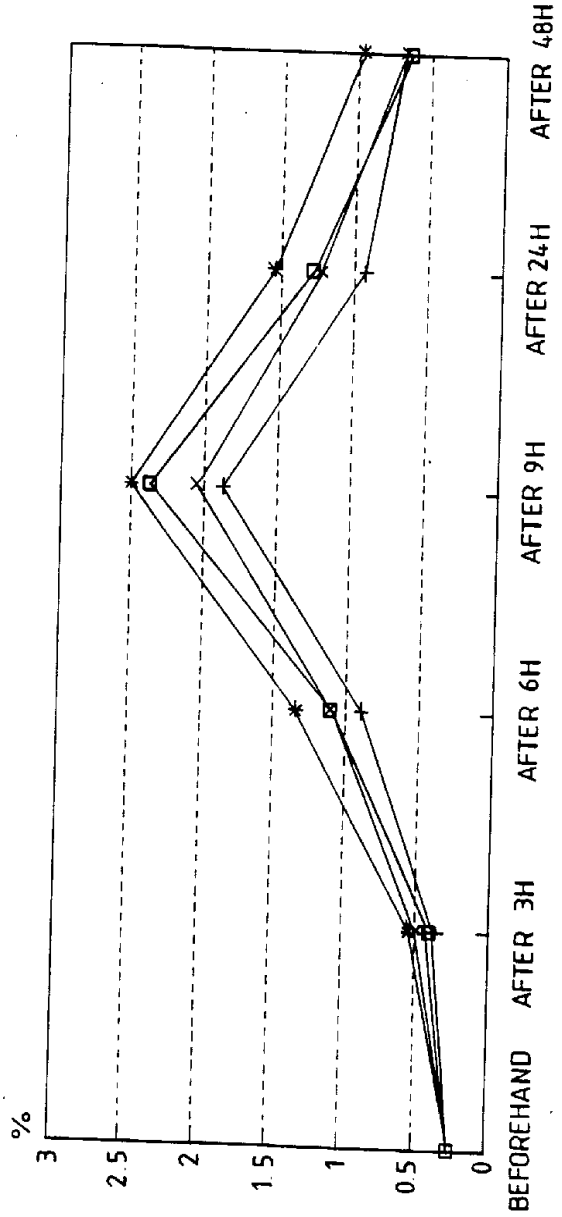
2.5
2
1.5
1
0.5
0
BEFOREHAND
AFTER 3H
AFTER 6H
AFTER 9H
AFTER 24H
AFTER48H
VM 196 (3% CAMOMILE)
CONTROL
HM 239 (2% CAMOMILE)
HM 349 (1% CAMOMILE)

Fig.1.


%
3
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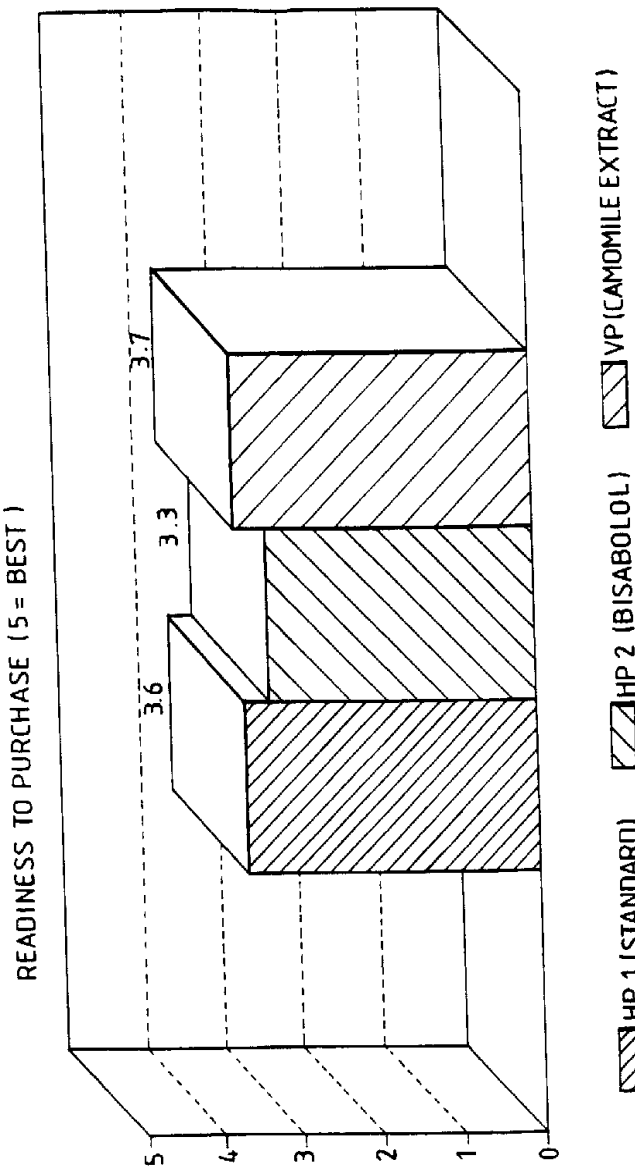
2
1.5
1
0.5
0
BEFOREHAND
AFTER 3H
AFTER 6H
AFTER 9H
AFTER 24H
AFTER 48H
HM 239 (2% CAMOMILE)
HP 1 (STANDARD)
CONTROL
HP 2 (BISABOLOL)

Fig.2.


READINESS TO PURCHASE (5 = BEST)
5
4
3
2
1
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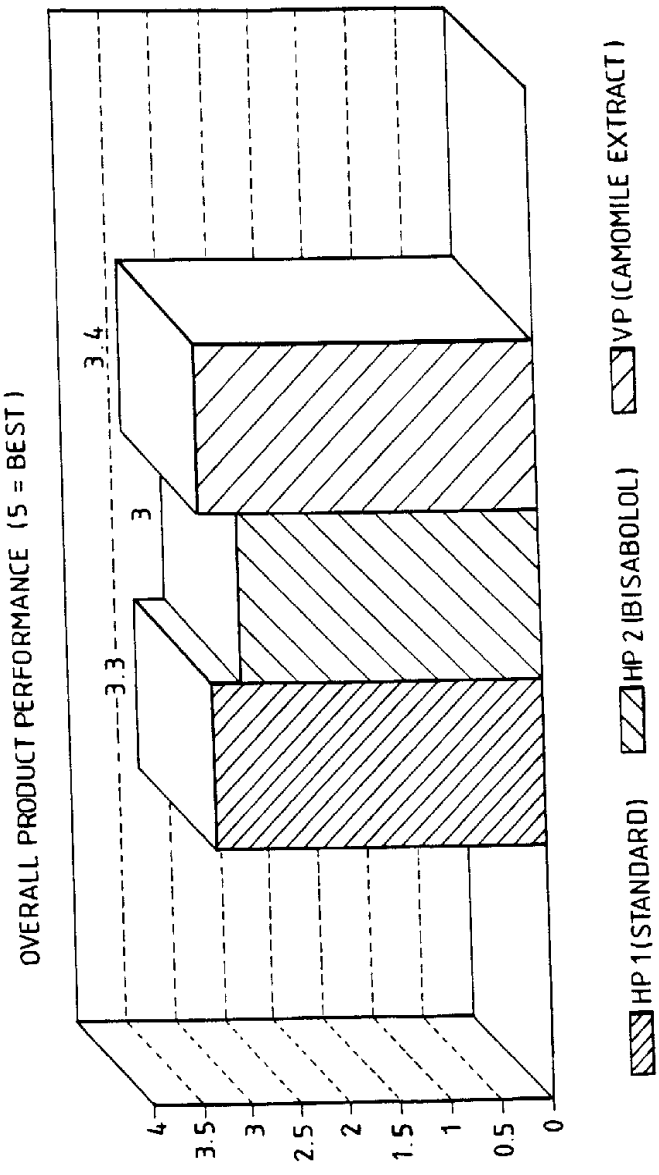
3.7
3.3
3.6
HP 1 (STANDARD)
HP 2 (BISABOLOL)
VP (CAMOMILE EXTRACT)

Fig.3.


OVERALL PRODUCT PERFORMANCE (5 = BEST)
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3.5
3
2.5
2
1.5
1
0.5
0
3.4
3
3.3
HP 1 (STANDARD)
HP 2 (BISABOLOL)
VP (CAMOMILE EXTRACT)

Fig.4.

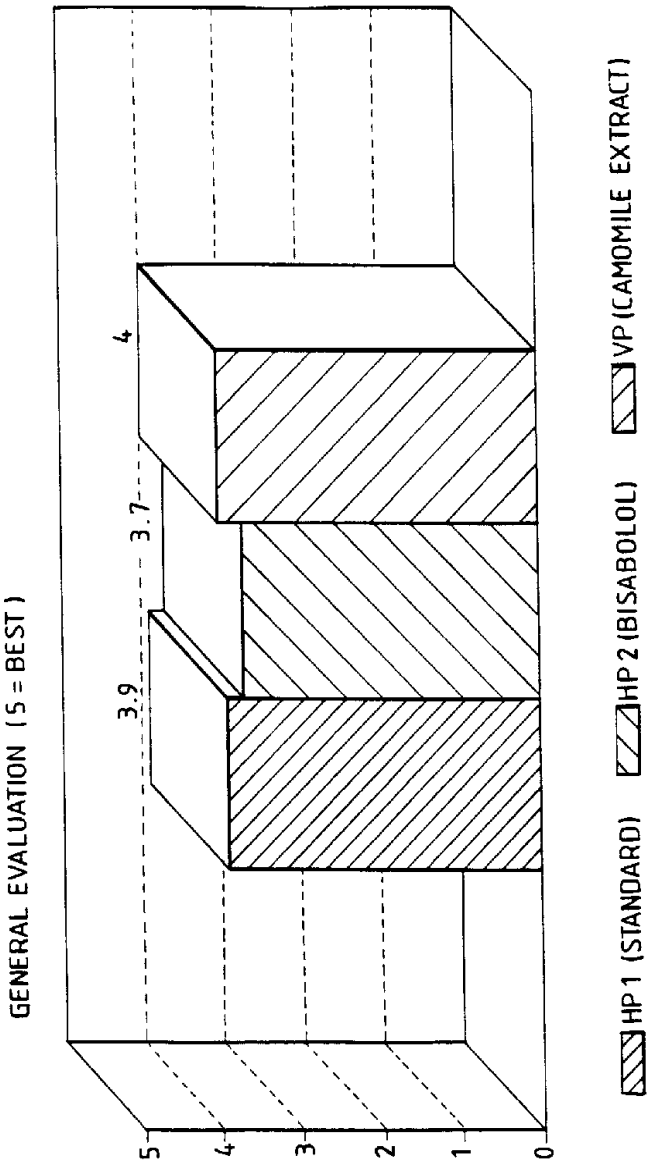
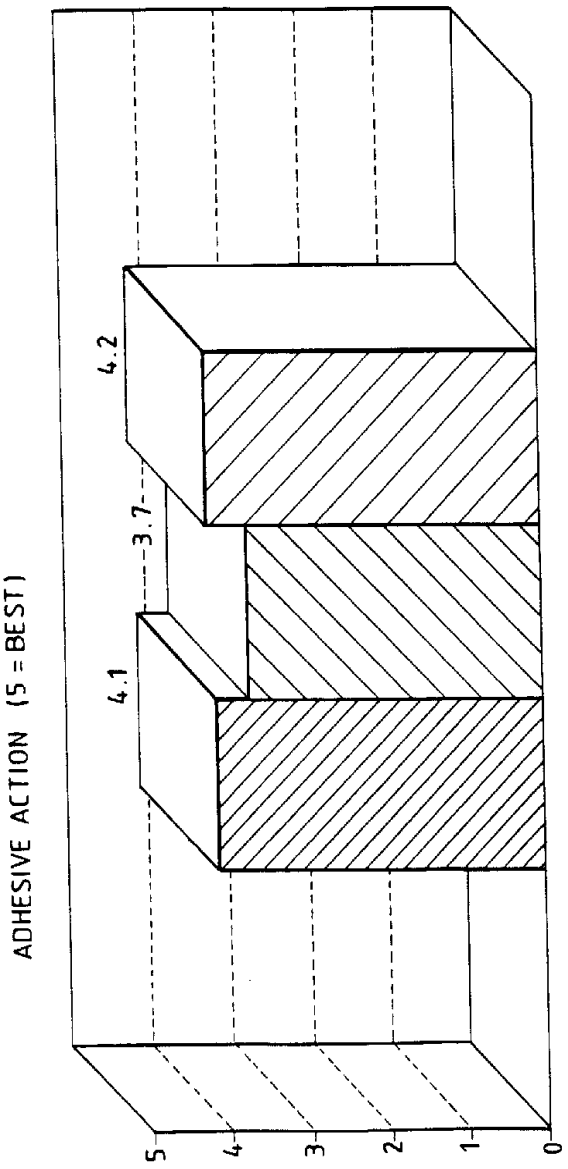

GENERAL EVALUATION (5 = BEST)
5
4
3
2
1
0
3.9
3.7
4
HP 1 (STANDARD)
HP 2 (BISABOLOL)
VP (CAMOMILE EXTRACT)

Fig.5.


ADHESIVE ACTION (5 = BEST)
4.2
3.7
4.1
5
4
3
2
1
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HP 1 (STANDARD)
HP 2 (BISABOLOL)
VP (CAMOMILE EXTRACT)

Fig.6.

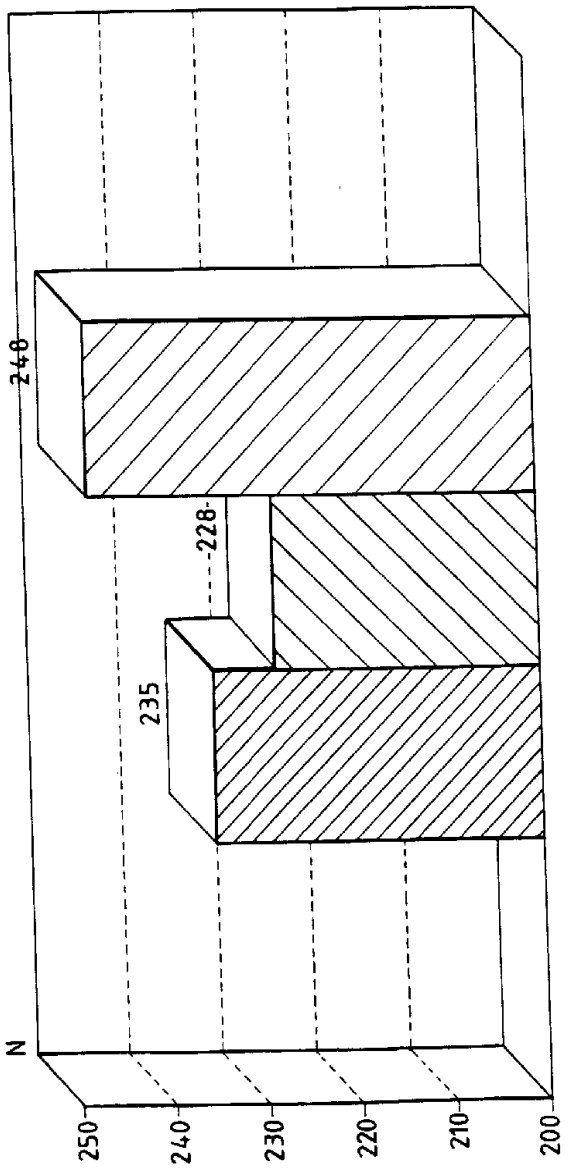
248
228
235
N
250
240
230
220
210
200
HP 1 (STANDARD)
HP 2 (BISABOLOL)
VP (CAMOMILE EXTRACT)

Fig. 7.